

CLAIMS

1. Medicinal combination of at least one immunosuppressive agent and at least one recombinant adenovirus whose genome comprises a first recombinant DNA containing a therapeutic gene and a second recombinant DNA containing an immunoprotective gene, for consecutive, intermittent and/or simultaneous use over time, which can be used for exogenous transfections in vivo and/or ex vivo.

2. Medicinal combination according to claim 1, characterized in that the immunosuppressive agent is preferably selected from among cyclosporin, FK506, azathioprine, corticosteroids and monoclonal or polyclonal antibodies.

3. Medicinal combination according to claim 2, characterized in that the antibodies concerned are antibodies which are able to inactivate immune molecules or induce destruction of the immune cells carrying these molecules.

4. Medicinal combination according to claim 3, characterized in that the antibody is selected from among the anti-CD4, -CD2, -CD3, -CD8, -CD28, -B7, -ICAM-1 and -LFA-1 antibodies and CTLA4Ig.

5. Medicinal combination according to one of the preceding claims, characterized in that the therapeutic gene encodes a therapeutic protein.

6. Medicinal combination according to one of claims 1 to 4, characterized in that the therapeutic gene

encodes a therapeutic RNA.

7. Medicinal combination according to one of the preceding claims, characterized in that the immunoprotective gene is a gene whose product acts on the activity of the major histocompatibility complex (MHC) or on the activity of the cytokines.

8. Medicinal combination according to claim 7, characterized in that the immunoprotective gene is a gene whose product at least partially inhibits expression of the MHC proteins or antigen presentation.

9. Medicinal combination according to one of the preceding claims, characterized in that the immunoprotective gene is selected from among the gene for gp19k of adenovirus, the ICP47 gene of herpes virus, or the UL18 gene of cytomegalovirus.

10. Medicinal combination according to one of the preceding claims, characterized in that the two recombinant DNAs of the adenovirus genome constitute a single transcriptional entity.

20            11. Medicinal combination according to one of  
the preceding claims, characterized in that the two  
recombinant DNAs each include an identical or different  
transcriptional promoter.

12. Medicinal combination according to claim  
25 11, characterized in that the two recombinant DNAs are  
inserted in the same orientation.

13. Medicinal combination according to claim 11, characterized in that the two recombinant DNAs are

inserted in opposite orientations.

14. Medicinal combination according to one of the preceding claims, characterized in that the two recombinant DNAs are inserted into one and the same site of the adenovirus genome, preferably within the E1, E3 or E4 regions.

15. Medicinal combination according to claim 14, characterized in that the two recombinant DNAs are inserted within the E1 region.

16. Medicinal combination according to one of claims 1 to 13, characterized in that the two recombinant DNAs are inserted into different sites in the adenovirus genome.

17. Medicinal combination according to claim 16, characterized in that one of the recombinant DNAs is inserted within the E1 region and the other within the E3 or E4 region.

18. Medicinal combination according to one of the preceding claims, characterized in that the adenovirus is a defective recombinant adenovirus which encompasses the ITR sequences and a sequence permitting encapsidation and which carries a deletion of all or part of the E1 and E4 genes.

19. Medicinal combination according to claim 18, characterized in that the adenovirus concerned is an adenovirus which encompasses the ITR sequences and a sequence permitting encapsidation and which carries a deletion of all or part of the E1, E3 and E4 genes.

20. Medicinal combination according to one of claims 1 to 19, characterized in that the adenovirus concerned is an adenovirus from whose genome all or part of the E1, E3, L5 and E4 genes have been deleted.

5 21. Medicinal combination according to one of the preceding claims, characterized in that the recombinant adenovirus is of human, animal or mixed origin.

10 22. Medicinal combination according to claim 21, characterized in that the recombinant adenoviruses of human origin are selected from among those classed within the C group, preferably from among the type 2 or type 5 recombinant adenoviruses (Ad 2 or Ad 5).

15 23. Medicinal combination according to claim 22, characterized in that the adenoviruses of animal origin are chosen from among the adenoviruses of canine, bovine, murine, ovine, porcine, avian and simian origin.

20 24. Medicinal combination according to one of the preceding claims, characterized in that the immunosuppressive agent is injected before and after injection of the adenovirus.

25 25. Medicinal combination according to one of the preceding claims, characterized in that the immunosuppressive agent and the recombinant adenovirus are injected simultaneously.

Add  
A1

Add  
C6

add E' >